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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/857,448

06/04/2001

Patrick Midoux

USB98ASIDM

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04/17/2006

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EXAMINER

SCHNIZER, RICHARD A

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/857,448	Applicant(s) MIDOUX ET AL.	
	Examiner Richard Schnizer, Ph. D	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25,26,28-34 and 36-41 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25,26,28-34 and 36-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

An amendment was received and entered on 1/26/06.

Claims 36-41 were added as requested.

Claims 25, 26, 28-34, and 36-41 remain pending and are under consideration in this Office Action.

All rejections from the previous Action which are not reiterated in this Action are withdrawn.

The rejection of claims 25 and 28-34 under 35 USC 103 is withdrawn because, as amended, these claims are so indefinite that they cannot be interpreted for examination under 35 USC 102 or 103. In contrast, claim 26, which depends from claim 25, has sufficient further limitations to render it interpretable.

Claim Objections

Claims 25 and 26 stand objected to. At page 17 of the response Applicant indicates that these claims were amended to address formal matters. However, it remains unclear as to whether or not the first structures set forth in claims 25 and 26 contain a negative charge on the right hand carboxyl group. This is due to a large number of black dots of approximately the same size as a negative charge notation next to the carboxyl group. As a result it is unclear whether or not the amendment of 7/11/05 introduced a negative charge sign, or merely deleted the previous, ambiguous black line adjacent to the carboxyl group. Also, in the PTO's copy of the claims, the character 'n' in the first formula of each of claims 25 and 26 remains illegible.

Claim 25 is also objected to because it is not properly marked-up to completely indicate all amendments. Specifically, on page 5, the phrase “which =h” is was deleted immediately following “-H,”, but this is not indicated as required by 37 CFR 1.121.

Claims 25 and 26 are also objected to because they appear to have incorporated a typographical error from the sentence bridging pages 4 and 5 of the previous Office Action. These claims state “wherein the total number of R' groups is equal to $p = q$ ”. (See claim 25 at page 4, and claim 26 at clause bridging pages 8 and 9.) However, it appears that R' must be equal to the sum of p and q, rather than being equal to each of p and q. That is, it appears that the claims should read “wherein the total number of R' groups is equal to $p + q$ ”, and not “ $p = q$.”

Claim 30 is objected to because “oligonucelotide” is misspelled in the penultimate line of the claim.

Claims 30 and 31 stand objected to because “conjugate” should be plural.

Claim 32 stand objected to because “osteoblats” and “cancel” are misspelled, and because the word “cells” should follow the words “muscular”, “epithelial”, “endothelial”, and “stem”.

Claim 36 is objected to because of improper subject/verb agreement. The word “is” should be substituted for the word “are” in the last line on page 11.

Claim 39 is objected to because the phrase “the R group identified as R” is unnecessary. Deletion of “identified as R” is suggested.

Claim 40 is objected to because “oligmre” is misspelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25, 26, and 28-34, and 36-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25, 28-34, and 36-41 are indefinite because the phrase “f is the number of groups that R is selected from the group consisting of”, at page 4 of the response, makes no sense. Did Applicant intend to transpose the words “that” and “R” so that the phrase read “f is the number of groups R that is selected from the group consisting of”? It is also unclear what is meant by “the number of NH_3^+ groups NH,” in the clause bridging pages 4 and 5. This is indefinite because NH is not an NH_3^+ group. In the claim as amended, it is unclear what is the difference between the variables ‘f’ and ‘j’. They both seem to be the number of NH_3^+ groups in the structure. Does the word “and” need to be inserted as the last word on page 4, or the first word on page 5? Claim 25 and dependents are also indefinite because the expression $i = u + j + k + h$ is invalid because ‘h’ is defined as a structure, not as a number. As a result the expression is meaningless, as is the expression $\text{omega } \text{NH}_3^+ = j = f - (k+h)$. This expression is also invalid because it appears that, as amended, the claim requires that $j = f$, so $j = f - (k+h)$ is only valid if k and h are both 0. It is also unclear where in the claimed conjugate the structures ‘h’ are located.

Claim 26 and dependents are indefinite because the phrase "selected from the group consisting are" at page 9, line 2 makes no sense.

Claim 36 is indefinite because it recites "the R group that are [sic] identified as U" without antecedent basis. There is no antecedent for 'U' (uppercase).

Claims 36-38 are indefinite because it is unclear what is intended by "(j) R = NH_3^+ ". It is unclear what is the effect of "(j)" in this expression.

Claims 39-41 are indefinite because it is unclear what is intended by "(k) R = NH-CO-CH_3 ". It is unclear what is the effect of "(k)" in this expression.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Midoux et al (WO 98/22610, published 5/28/98).

WO 98/22610 was filed as PCT/FR97/02022 and is the priority document for US Patent 6,372,499. The contents of WO 98/22610 will be discussed by reference to this English language version. Midoux teaches oligomers with a polymerization degree as low as 15, in which at least 10% of the monomers have free NH_3^+ groups substituted by residues that are protonable in a weak acid medium, such as histidines, pterines, quinolines, or pyridines, leading to destabilization of cell membranes. See entire

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document, e.g. abstract; column 4, lines 20-24; column 4, line 55 to column 5, line 40; column 6, line 48 to column 8, line 43; and column 10, line 44 to column 11, line 38.

The R groups recited in the claims are set forth at e.g. column 10 line 44 to column 12 line 22, wherein $m = 1$, n is from 1-6, n' and n'' are both = 0, and B is an imidazole group. Instant R' is NH_3^+ .

It is noted that the instant claims require at least 50% substitution. However, the recited "at least 10%" in the cited art is reasonably interpreted as embracing 10% to 100%, so the instantly claimed "at least 50%" is embraced by the range in the cited art. As such it would have been obvious to one of ordinary skill in the art to arrive at the claimed conditions through the process of routine optimization within the range in the cited art. Note that the instant application shows that the instant invention functions to deliver polynucleotides when the level of substitution is 53%. See Table 1 on page 39.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 8/8/05 have been fully considered as they apply to the rejections set forth above, but they are not persuasive.

At page 19 of the response Applicant asserts that WO 98/22610 does not disclose enough information to allow one skilled in the art to choose a degree of polymerization and a percentage of substitution of oligomers to transfer oligonucleotides as recited in the instant claim. This is unpersuasive because the rejected claim does not require transfer of oligonucleotides. Instead, it is drawn to an oligomeric conjugate

with a peptide backbone. Even if the claim required oligonucleotides, it would still be obvious for the reasons of record. Applicant states that table 1 at specification page 39 shows that when the degree of polymerization is 36 to 190 and histidine substitution is less than 50% transfection with DNA is very efficient, but transfection with oligonucleotides is inefficient. Applicant states that this degree of polymerization is higher than that of the present invention, and that the degree of histidine substitution is higher than the limit of the cited art. This is unpersuasive for several reasons. First, Applicant admits that the use of a 36mer with 53% histidine substitution is operational. The opinion that it is inefficient does not render the claim non-obvious. Second, Applicant's statement that a degree of polymerization of 36 is higher than that instantly claimed is incorrect. The instant claims allow a oligomer of 36 monomers. See claim 1, which describes an oligomer of 34 core monomers and 2 terminal monomers. Applicant's statement that the degree of histidine substitution is higher than the limit of the cited art is also incorrect. The cited art taught oligomers with a polymerization degree as low as 15, in which **at least 10%** of the monomers have free NH₃⁺ groups substituted by residues that are protonable in a weak acid medium. Thus the degree of substitution is reasonably interpreted as embracing 10-100%, and so overlaps the claimed range of at least 50%. MPEP 2144 states "[i]n the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)."

For these reasons the rejection is maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax

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number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

A handwritten signature in black ink, appearing to read 'Richard Schnizer', with a long horizontal line extending to the right.

Richard Schnizer, Ph.D.
Primary Examiner
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